## FUNCTIONAL SYMPTOMS HAVE A NEUROBIOLOGICAL SUBSTRATE BASED ON ADAPTATION TO ENVIRONMENTAL CHALLENGES AND STRESS TOWARDS A NEUROBIOLOGICAL MODEL OF FUNCTIONAL AMNESIA Angelica Staniloiu

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Once seen as the opposite of so-called "organic" amnesia, the term functional amnesia nowadays refers to amnes(t)ic disorders that occur without evidence of significant brain damage as detected by conventional structural brain imaging techniques and have an unsure etiology. When brain damage exists, the extent of memory impairments cannot be accounted for by the locus and degree of brain damage and functional amnesia is often labeled as "disproportionate amnesia". Although several authors use the terms psychogenic, dissociative or functional amnesia interchangeably, there are subtle differences among them. The term dissociative amnesia by definition designates a form of psychogenic amnesia underlain by the psychological mechanism of dissociation, while psychogenic amnesia refers to amnes(t)ic disorders that are etiologically linked to a larger gamut of psychological mechanisms. Functional amnesia often occurs on background of psychological stress or trauma, alone or in combination with a co-occurring (mild) physical insult (such as a mild traumatic brain injury, mild electrocuting accident or a mild physical injury). There are however case-reports of functional amnesia where a clear-cut psychological etiological mechanism could not be identified. The lack of clearly identifiable psychological triggers in these variants of functional amnesia might be accounted for by several factors, such as: memory disturbance for the stressful event due to amnesia; an impaired capacity for emotional awareness and processing in the face of ongoing or recurrent stresses that seems to premorbidly characterize some of the patients with psychogenic amnesia and in fact might predispose them to develop this condition; the possible involvement of mechanisms of kindling sensitization in the face of repeated stresses, which may trigger an episode of illness after a seemingly objective minor stress; the so called incubation effect of life adversity (Staniloiu and Markowitsch, 2010). The memory impairment in functional amnesia is usually of a retrograde nature, but might at times be anterograde as well. The memory impairment does not occur in isolation, but is often accompanied by impairments of executive functions, theory of mind functions, emotional processing, self-consciousness and mental time travelling.

Since the advent of functional imaging, research data have increasingly been providing evidence in functional amnesia of functional and metabolic changes in brain areas that are agreed upon to exert a crucial role in memory processes. The differences in the localization and nature of the changes, which were at times reported, might be accounted for by several factors, such as the individual characteristics of the patients, the lack of control for variables, such as sex, differences in methodology (types of imaging methods used, the performance of functional imaging during rest versus administration of various tasks, differences in the task paradigms employed, etc). In a study in which glucose-PET data obtained during resting state from 14 patients with dissociative or functional amnesia and severe episodic-autobiographical memory deficits were analyzed in combination, it was found that the right temporo-frontal region was hypometabolic in a significant number of patients, with a significant reduction in the right inferolateral prefrontal cortex (Brand et al., 2009). These results provide support for the pathogenetic model of functional amnesia that had been advanced by Markowitsch and co-workers. This model has posited that the recollection deficit in functional or psychogenic amnesia primarily reflects a stress hormone-triggered and -mediated memory blockade, underpinned by a desynchronization during retrieval between the frontal lobe system, important for autonoetic consciousness, and the temporo-amygdalar system, important for emotional processing and colorization (Markowitsch, 2002).

The recent broader use of imaging techniques such as diffusion tensor imaging or magnetization-transfer ratio measurements began to provide evidence in functional amnesia of subtle micro-structural changes of fiber tracts involved in mnemonic processing, posing therefore a challenge to the validity of the concept of "functional". A further challenge to this concept comes from recent data showing that, in contrast to old perceptions of functional amnesia as a reversible condition, in a substantial number of patients with functional amnesia the (episodic-autobiographical) memory impairments follow a chronic, unremitting course. Furthermore, in some cases there may be further cognitive deterioration over time, though prospective larger scale studies are missing. There are currently no evidence-based treatments for functional amnesia. This suggests that further research focused on disentangling the neurobiological correlates of this condition is needed. This research might be enabled by the combined employment of functional and newer structural imaging techniques and refined use of rigorous neuropsychological methodology.

## References

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